PATENT
0030-0208P

IN THE U.S. PATENT AND TRADEMARK OFFICE

APPLICANT:	Marcus KEEP, et al.	CONF.:	4570
SERIAL NO:	10/757,533	GROUP:	1631
FILED:	January 15, 2004	EXAMINER:	BORIN
FOR:	NEUROIMMUNOPHILINS FOR SELECTIVE NEURONAL RADIOPROTECTION		

LETTER TO FILE

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

March 10, 2006

Sir:

Previously (on January 10, 2005), Applicants had cited WO 96/22104 A1 in the file of the above-identified application. Applicants enclose herewith a copy of pages from a Communication from the European Patent Office, which communication discusses the previously-cited reference WO 96/22104 A1.

If the Examiner has any questions concerning this application, he is requested to contact Richard Gallagher, Reg. No. 28,781, at (703) 205-8008.

Respectfully submitted,
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Application No.	Ref.	Date
98 948 530.5 - 1521	EP 21079-019/zp	07.12.2006
Applicant: Keep, Marcus		

Communication pursuant to Article 96(2) EPC

The examination of the above-identified application has revealed that it does not meet the requirements of the European Patent Convention for the reasons enclosed herewith. If the deficiencies indicated are not rectified the application may be refused pursuant to Article 97(1) EPC.

You are invited to file your observations and insofar as the deficiencies are such as to be rectifiable, to correct the indicated deficiencies within a period

of 4 months

from the notification of this communication, this period being computed in accordance with Rules 78(2) and 83(2) and (4) EPC.

One set of amendments to the description, claims and drawings is to be filed within the said period on separate sheets (Rule 36(1) EPC).

Failure to comply with this invitation in due time will result in the application being deemed to be withdrawn (Article 96(3) EPC).

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Fuchs, U
Primary Examiner
for the Examining Division

Enclosure(s): 4 page/s reasons (Form 2906)

Registered Letter
EPO Form 2001 07.02CSX

Bescheid/Protokoll (Anlage)	Communication/Minutes (Annex)	Notification/Procès-verbal (Annexe)
Datum Date Date 07.12.2005	Blatt Sheet Feuille 1	Anmelde-Nr.: Application No.: 98 948 530.5 Demande n°:

The examination is being carried out on the **following application documents**:

Description, Pages

1-17 as originally filed

Claims, Numbers

1-17 received on 17.04.2001 with letter of 17.04.2001

Reference is made to the following document; the numbering will be adhered to in the rest of the procedure:

D1: WO 96/22104 A (ELMER, E. ET AL.), 25 July 1996

1. Clarity and Support (Article 84 EPC), Patentability (Article 52(4) EPC)

1.1 In present application the use of neuroimmunophilin ligands for the manufacture of medicament for the radiotherapy of primary brain tumors, metastatic brain tumors and lesions is claimed. Examples 1-14 describe possible therapies involving such uses and examples 15-27 list possible neuroimmunophilin ligand formulations. However, there is no experimental evidence disclosed supporting the alleged effect of neuroimmunophilin ligands on the above listed pathological conditions.

Accordingly, the subject-matter of **claims 1-17** might be regarded as not supported by the description in the sense of Article 84 EPC.

1.2 The second medical use **claims 1-3** are not acceptable under Article 84 EPC. The

therapeutic application is functionally defined by a mechanism of action which does not allow any practical application in the form of a defined, real treatment of a pathological condition (disease) (Guidelines C-IV, 4.2 and C-III, 4.14).
The objection could be overcome by either introducing in the claims a list of pathological conditions (diseases) cited in the application, or by showing that means are available which would allow the skilled person to recognise which additional condition(s) would fall within the functional definition.

1.3 Claim 15 with the present wording is a mixed first medical use ("use as an effective neuron radioprotectant treatment") / second medical use ("for the manufacture of a medicament for ...") claim (Guidelines C-IV, 4.2).

In view of the fact that the pharmaceutically active substances of present application are known for use in therapy, the claim should be amended to form a second medical use type of claim.

1.4 Claim 16 relates to an article of manufacture comprising packaging material, the pharmaceutically active substances of present application and a "label which indicates that the pharmaceutical agent can be used for ...". It is to be noted that such a label is a non-technical feature providing no technical contribution to the claimed product and that is does not limit the scope of such the claim, i.e. that it does not have to be considered in the evaluation of novelty (see **item 2**).

1.5 The subject-matter of present **claim 17** refers to a method for treatment of the human body by therapy and is therefore excluded from patentability under Article 52(4) EPC (Guidelines C-IV, 4.2).

1.6 The vague and imprecise statement in the description on page 10, line 36 - page 11, line 9 implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity of the claims when used to interpret them (Guidelines, C-III, 4.3a). This statement should therefore be deleted to remove this inconsistency.

1.7 The references mentioned on the page preceding the description should be

incorporated into the description. The further, redundant information should be deleted.

2. Novelty (Article 54 EPC)

D1 discloses the use of neuroimmunophilin ligands like cyclosporins, especially cyclosporin A, derivatives, metabolites, variants, or salts thereof for the manufacture of a pharmaceutical composition for the prevention or treatment of mammal neuron damage or death caused by e.g. radiation (see page 3, paragraph 4; page 4, paragraph 3). The neuroimmunophilin ligands could be administered before, simultaneously or after the neuron damage (see page 8, paragraphs 2, 3) by several routes like intravenous, intra arterial, parenteral, intra parenchymal, via cerebrospinal fluid spaces, intra ventricular fluid spaces, or by application into digestive, respiratory, genitourinary systems or to the skin (see page 7, paragraph 2). The use of the neuroimmunophilin ligands in the context of the treatment of brain lesions is also proposed (see page 8, line 21).

Consequently, and notwithstanding the objections made under **Items 1.1-1.5**, the subject-matter of **claims 1-7, 14-17** lacks novelty.

3. Inventive Step (Article 56 EPC)

Independent of the above novelty objection, subject-matter of claims 1-17 cannot be recognized as involving an inventive step, since it has not been demonstrated that the problem underlying the present application, which can be defined as the provision of further neuroimmunophilin ligands for use as a medicament in the prevention or treatment of mammal neuron damage or death caused by radiation, has indeed been solved by the application. Although the application speculates that the claimed neuroimmunophilin ligands might be effective as neuroprotectant against damage caused by radiation, no evidence whatsoever has been presented to support this hypothesis (see **item 1.1**). Since

the above mentioned problem cannot be recognized as having been solved by the application, no inventive step can be acknowledged for the subject-matter of **claims 1-17.**

The applicant is requested to provide evidence supporting his hypothesis, e.g. by presenting experimental data.

4. Prior Art (Rule 27(1)(b) EPC)

To meet the requirements of Rule 27(1)(b) EPC, the document **D1** should be identified in the description and its relevant contents should be indicated.

5. Conclusions

The applicant is requested to file new claims which take account of the above comments.

Further, the applicant is requested to provide evidence supporting his hypothesis.

When filing amended claims the applicant should at the same time bring the description into conformity with the amended claims. Care should be taken during revision not to add subject-matter which extends beyond the content of the application as originally filed (Article 123(2) EPC).

In order to facilitate the examination of the conformity of the amended application with the requirements of Article 123(2) EPC, the applicant is requested to clearly identify the amendments carried out, irrespective of whether they concern amendments by addition, replacement or deletion, and to indicate the passages of the application as filed on which these amendments are based. If the applicant regards it as appropriate these indications could be submitted in handwritten form on a copy of the relevant parts of the application as filed.

also in the preamble of the claims. Reference signs should not however be seen as limiting the extent of the matter protected by the claims; their sole function is to make claims easier to understand. A comment to that effect in the description is acceptable (see T 237/84, OJ 7/1987, 309).

If text is added to reference signs in parentheses in the claims, lack of clarity can arise (Art. 84). Expressions such as "securing means (screw 13, nail 14)" or "valve assembly (valve seat 23, valve element 27, valve seat 28)" are not reference signs in the sense of Rule 29(7) but are special features, to which the last sentence of Rule 29(7) is not applicable. Consequently, it is unclear whether the features added to the reference signs are limiting or not. Accordingly, such bracketed features are generally not permissible. However, additional references to those figures where particular reference signs are to be found, such as "(13 - Figure 3; 14 - Figure 4)", are unobjectionable.

A lack of clarity can also arise with bracketed expressions that do not include reference signs, e.g. "(concrete) moulded brick". In contrast, bracketed expressions with a generally accepted meaning are allowable, e.g. "(meth)acrylate" which is known as an abbreviation for "acrylate and methacrylate". The use of brackets in chemical or mathematical formulae is also unobjectionable.

4.12 Negative limitations (e.g. disclaimers)

A claim's subject-matter is normally defined in terms of positive features indicating that certain technical elements are present. Exceptionally, however, the subject-matter may be restricted using a negative limitation expressly stating that particular features are absent. This may be done e.g. to remove non-patentable embodiments disclosed in the application as filed (see T 4/80, OJ 4/1982, 149) or if the absence of a feature can be deduced from the application as filed (see T 278/88, not published in OJ).

Negative limitations such as disclaimers may be used only if adding positive features to the claim either would not define more clearly and concisely the subject-matter still protectable (see T 4/80, OJ 4/1982, 149) or would unduly limit the scope of the claim (see T 1050/93, not published in OJ).

With respect to the allowability of a disclaimer not disclosed in the application as filed, see VI, 5.3.11.

4.13 "Comprising" vs. "consisting"

While in everyday language the word "comprise" may have both the meaning "include", "contain" or "comprehend" and "consist of", in drafting patent claims legal certainty normally requires it to be interpreted by the broader meaning "include", "contain" or "comprehend". On the other hand, if a claim for a chemical compound refers to it as "consisting of components A, B and C" by their proportions expressed in percentages, the presence of any additional component is excluded and therefore the percentages should add up to 100% (see T 759/91 and T 711/90, both not published in OJ).

4.14 Functional definition of a pathological condition

When a claim is directed to a further therapeutic application of a medicament and the condition to be treated is defined in functional terms, e.g. "any condition susceptible of being improved or prevented by selective

occupation of a specific receptor", the claim can be regarded as clear only if instructions, in the form of experimental tests or testable criteria, are available from the patent documents or from the common general knowledge allowing the skilled person to recognise which conditions fall within the functional definition and accordingly within the scope of the claim (T 241/95, OJ 2/2001, 103) (see also IV, 4.2).

5. Conciseness, number of claims

Art. 84
Rule 29(5)

The requirement that the claims must be concise refers to the claims in their entirety as well as to the individual claims. The number of claims must be considered in relation to the nature of the invention the applicant seeks to protect. Undue repetition of wording, e.g. between one claim and another, should be avoided by the use of the dependent form. Regarding independent claims in the same category see III, 3.2 and 3.3. As for dependent claims, while there is no objection to a reasonable number of such claims directed to particular preferred features of the invention, the examiner should object to a multiplicity of claims of a trivial nature. What is or what is not a reasonable number of claims depends on the facts and circumstances of each particular case. The interests of the relevant public must also be borne in mind. The presentation of the claims should not make it unduly burdensome to determine the matter for which protection is sought (T 79/91 and T 246/91, not published in OJ). Objection may also arise where there is a multiplicity of alternatives within a single claim, if this renders it unduly burdensome to determine the matter for which protection is sought.

6. Support in description

6.1 General remarks

Art. 84

The claims must be supported by the description. This means that there must be a basis in the description for the subject-matter of every claim and that the scope of the claims must not be broader than is justified by the extent of the description and drawings and also the contribution to the art (T 409/91, OJ 9/1994, 653). Regarding the support of dependent claims by the description, see III, 6.6.

6.2 Extent of generalisation

Most claims are generalisations from one or more particular examples. The extent of generalisation permissible is a matter which the examiner must judge in each particular case in the light of the relevant prior art. Thus an invention which opens up a whole new field is entitled to more generality in the claims than one which is concerned with advances in a known technology. A fair statement of claim is one which is not so broad that it goes beyond the invention nor yet so narrow as to deprive the applicant of a just reward for the disclosure of his invention. The applicant should be allowed to cover all obvious modifications of, equivalents to and uses of that which he has described. In particular, if it is reasonable to predict that all the variants covered by the claims have the properties or uses the applicant ascribes to them in the description, he should be allowed to draw his claims accordingly. After the date of filing, however, he should be allowed to do so only if this does not contravene Art. 123(2).

6.3 Objection of lack of support

As a general rule, a claim should be regarded as supported by the description unless there are well-founded reasons for believing that the skilled person would be unable, on the basis of the information given in

4. Industrial application

4.1 General remarks

Art. 57

"An invention shall be considered as susceptible of industrial application if it can be made or used in any kind of industry, including agriculture". "Industry" should be understood in its broad sense as including any physical activity of "technical character" (see IV, 1.2), i.e. an activity which belongs to the useful or practical arts as distinct from the aesthetic arts; it does not necessarily imply the use of a machine or the manufacture of an article and could cover e.g. a process for dispersing fog or for converting energy from one form to another. Thus, Art. 57 excludes from patentability very few "inventions" which are not already excluded by the list in Art. 52(2) (see IV, 2.1). One further class of "invention" which would be excluded, however, would be articles or processes alleged to operate in a manner clearly contrary to well-established physical laws, e.g. a perpetual motion machine. Objection could arise under Art. 57 only insofar as the claim specifies the intended function or purpose of the invention; but if, say, a perpetual motion machine is claimed merely as an article having a particular specified construction then objection should be made under Art. 83 (see II, 4.11).

4.2 Surgery, therapy and diagnostic methods

Art. 52(4)

"Methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body shall not be regarded as inventions which are susceptible of industrial application. This provision shall not apply to products, in particular substances or compositions, for use in any of these methods." Hence, patents may be obtained for surgical, therapeutic or diagnostic instruments or apparatuses for use in such methods. The manufacture of prostheses or artificial limbs could be patentable. For instance, a method of manufacturing insoles in order to correct the posture or a method of manufacturing an artificial limb should be patentable. In both cases, taking the imprint of the footplate or a moulding of the stump on which an artificial limb is fitted is clearly not of a surgical nature and does not require the presence of a medically qualified person. Furthermore, the insoles as well as the artificial limb are manufactured outside the body. However, a method of manufacturing an endoprosthesis outside the body, but requiring a surgical step to be carried out for taking measurements, would be excluded from patentability under Art. 52(4) EPC (see T 1005/98, not published in OJ).

Art. 54(5)

Patents may also be obtained for new products for use in these methods of treatment or diagnosis, particularly substances or compositions. However, in the case of a known substance or composition, this may only be patented for use in these methods if the known substance or composition was not previously disclosed for use in surgery, therapy or diagnostic methods practised on the human or animal body ("**first medical use**"). The same substance or composition cannot subsequently be patented for any other use of that kind. A claim to a known substance or composition for the first use in surgical, therapeutic and/or diagnostic methods should be in a form such as: "Substance or composition X" followed by the indication of the use, for instance "... for use as a medicament", "... as an antibacterial agent" or "... for curing disease Y". In contrast to what is stated in general in III, 4.8, these types of claims will be regarded as restricted to the substance or composition when presented or packaged for the use. Art. 54(5) thus provides for an exception from the general principle that product claims can only be obtained for (absolutely) novel products. However, this does not mean that product claims for the

first medical use need not fulfil all other requirements of patentability, especially that of inventive step (see T 128/82, OJ 4/1984, 164).

A claim in the form "Use of substance or composition X for the treatment of disease Y ..." will be regarded as relating to a method for treatment explicitly excluded from patentability by Art. 52(4) and therefore will not be accepted.

If an application discloses for the first time a number of distinct surgical, therapeutic or diagnostic uses for a known substance or composition, normally in the one application independent claims each directed to the substance or composition for one of the various uses may be allowed; i.e. an a priori objection of lack of unity of invention should not, as a general rule, be raised (see III, 7.6). Art. 82

A claim in the form "Use of a substance or composition X for the manufacture of a medicament for therapeutic application Z" is allowable for either a first or "subsequent" (second or further) such application ("**second medical use**"-type of claim or "Swiss-type" claim), if this application is new and inventive (cf. G 5/83, OJ 3/1985, 64). The same applies to claims in the form "Method for manufacturing a medicament intended for therapeutic application Z, characterised in that the substance X is used" or the substantive equivalents thereof (see T 958/94, OJ 6/1997, 241). In cases where an applicant simultaneously discloses more than one "subsequent" therapeutic use, claims of the above type directed to these different uses are allowable in the one application, but only if they form a single general inventive concept (Art. 82). Regarding use or method claims of the above type, it should also be noted that a mere pharmaceutical effect does not necessarily imply a therapeutical application. For instance, the selective occupation of a specific receptor by a given substance cannot be considered in itself as a therapeutic application; indeed, the discovery that a substance selectively binds a receptor, even if representing an important piece of scientific knowledge, still needs to find an application in the form of a **defined, real** treatment of a pathological condition in order to make a technical contribution to the art and to be considered as an invention eligible for patent protection (see T 241/95, OJ 2/2001, 103). See also III, 4.14, for the functional definition of a pathological condition.

4.2.1 Limitations of exclusion under Art. 52(4)

It should be noted that Art. 52(4) excludes only methods of treatment by surgery or therapy and diagnostic methods. It follows that other methods of treatment of live human beings or animals (e.g. treatment of a sheep in order to promote growth, to improve the quality of mutton or to increase the yield of wool) or other methods of measuring or recording characteristics of the human or animal body are patentable provided that (as would probably be the case) such methods are of a technical and not essentially biological character (see IV, 3.4) and are susceptible of industrial application. The latter proviso is particularly important in the case of human beings. For example, an application with a claim for a method of contraception, which is to be applied in the private and personal sphere of a human being, is not susceptible of industrial application (see T 74/93, OJ 10/1995, 712). However, an application containing claims directed to the purely cosmetic treatment of a human by administration of a chemical product is considered as being susceptible of industrial application (see T 144/83, OJ 9/1986, 301). A cosmetic treatment involving surgery or therapy would, however, not be patentable (see below). Art. 52(4)

In order to be excluded, a treatment or diagnostic method must actually be carried out on the living human or animal body. A treatment of or diagnostic method practised on a dead human or animal body would therefore not be excluded from patentability by virtue of Art. 52(4). Treatment of body tissues or fluids after they have been removed from the human or animal body, or diagnostic methods applied thereon, are not excluded from patentability insofar as these tissues or fluids are not returned to the same body. Thus the treatment of blood for storage in a blood bank or diagnostic testing of blood samples is not excluded, whereas a treatment of blood by dialysis with the blood being returned to the same body would be excluded.

Regarding methods which are carried out on or in relation to the living human or animal body, it should be borne in mind that the intention of Art. 52(4) is only to free from restraint non-commercial and non-industrial medical and veterinary activities. Interpretation of the provision should avoid the exclusions from going beyond their proper limits (see G 5/83, OJ 3/1985, 64).

However, in contrast to the subject-matter referred to in Art. 52(2) and (3) which is only excluded from patentability if claimed as such, a method claim is not allowable under Art. 52(4) if it includes at least one feature defining a physical activity or action that constitutes a method step for treatment of the human or animal body by surgery or therapy or a diagnostic method step to be exercised on the human or animal body. In that case, whether or not the claim includes or consists of features directed to a technical operation performed on a technical object is legally irrelevant to the application of Art. 52(4) (see T 820/92, OJ 3/1995, 113, and T 82/93, OJ 5/1996, 274).

Taking the three exclusions in turn:

Surgery defines the nature of the treatment rather than its purpose. Thus, for example, a method of treatment by surgery for cosmetic purposes or for embryo transfer is excluded, as well as surgical treatment for therapeutic purposes.

Therapy implies the curing of a disease or malfunction of the body and covers prophylactic treatment, e.g. immunisation against a certain disease (see T 19/86, OJ 1-2/1989, 24) or the removal of plaque (see T 290/86, OJ 8/1992, 414). A method for therapeutic purposes concerning the functioning of an apparatus associated with a living human or animal body is not excluded if no functional relationship exists between the steps related to the apparatus and the therapeutic effect of the apparatus on the body (see T 245/87, OJ 5/1989, 171).

Diagnostic methods likewise do not cover all methods related to diagnosis. Methods for obtaining information (data, physical quantities) from the living human or animal body are not excluded by Art. 52(4), if the information obtained merely provides intermediate results which, on their own, do not enable a decision to be made on the treatment necessary. Generally such methods include X-ray investigations, NMR studies, and blood pressure measurements (see T 385/86, OJ 8/1988, 308).

4.3 Method of testing

Methods of testing generally should be regarded as inventions susceptible of industrial application and therefore patentable if the test is applicable to the improvement or control of a product, apparatus or process which is